

Supplementary Appendix

Supplement to: Age-specific patterns of enteropathogenic infections and co-infections among patients with different severity of acute diarrhea in China from 2009 to 2020

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Supplementary table 1. Modified Vesikari Score method for the classification of diarrhea cases*.

Variable	Score			
	0	1	2	3
Duration of diarrhea before admission (day)	0	1–4	5	≥6
Average number of episodes per day before admission for diarrheal stools	0	1–3	4–5	≥6
Duration of vomiting before admission (day)	0	1	2	≥3
Average number of episodes per day before admission for vomiting	0	1	2–4	≥5
Body temperature upon admission	<37.0 °C	37.1–38.4 °C	38.5–38.9 °C	≥39.0 °C
Healthcare provider visits	None		Outpatient	Emergency Department
Status of treatment received	None	Oral rehydration before admission	Hospitalization	

*Deaths are also included and were defined as cases of moderate to severe diarrhea.

Supplementary table 2. Demographic characteristics of deaths and non-deaths of diarrheal patients in the mainland of China, 2009–2020

	Total (n=195,988)	Death (n=63)	Non-death (n=195,925)	P value
Sex				0.9476
Female	80,126 (40.88)	25 (39.68)	80,101 (40.88)	
Male	115,862 (59.12)	38 (60.32)	115,824 (59.12)	
Age				0.7041
<6 month	22,199 (11.33)	7 (11.11)	22,192 (11.33)	
6–11 month	28,487 (14.54)	7 (11.11)	28,480 (14.54)	
1–4 years	45,927 (23.43)	15 (23.81)	45,912 (23.43)	
5–17 years	12,804 (6.53)	4 (6.35)	12,800 (6.53)	
18–59 years	65,027 (33.18)	19 (30.16)	65,008 (33.18)	
≥60 years	21,544 (10.99)	11 (17.46)	21,533 (10.99)	
Ecological regions				0.5217
North China	45,714 (23.32)	17 (26.98)	45,697 (23.32)	
Northeast China	9,211 (4.70)	0 (0.00)	9,211 (4.70)	
South China	24,642 (12.57)	9 (14.29)	24,633 (12.57)	
Inner Mongolia-Xinjiang	12,914 (6.59)	6 (9.52)	12,908 (6.59)	
Qinghai-Tibet	1,443 (0.74)	0 (0.00)	1,443 (0.74)	
Southwest China	7,958 (4.06)	2 (3.17)	7,956 (4.06)	
Central China	94,106 (48.02)	29 (46.03)	94,077 (48.02)	
Residence				0.2278
Urban	153,786 (78.47)	45 (71.43)	153,741 (78.47)	
Rural	42,202 (21.53)	18 (28.57)	42,184 (21.53)	
Season of infection				>0.9999
Cold	75,614 (38.58)	24 (38.10)	75,590 (38.58)	
Warm	120,374 (61.42)	39 (61.90)	120,335 (61.42)	
Case type				0.0225
Outpatient	182,079 (92.90)	63 (100.00)	182,016 (92.90)	
Inpatient	13,909 (7.10)	0 (0.00)	13,909 (7.10)	

Data are presented as n (%). *p value was compared between death group and non-death group based on chi-square test or Fisher’s exact test.

Supplementary table 3. Positive rate of gastrointestinal pathogens among patients with mild diarrhea and MSD by age group, gender, residence, and season of infection in the mainland of China, 2009–2020.

	Age group													
	Total		<6 months		6–11 months		1–4 years		5–17 years		18–59 years		≥60 years	
	Mild	MSD	Mild	MSD	Mild	MSD	Mild	MSD	Mild	MSD	Mild	MSD	Mild	MSD
Virus	18,974 (28.35)	5,752 (46.45) **	2,307 (29.24)	538 (42.87) **	4,104 (41.41)	1,593 (57.63) **	6,591 (41.37)	2,699 (57.38) **	950 (23.16)	211 (30.89) **	3,796 (17.76)	531 (23.71) **	1,226 (15.89)	180 (24.39) **
Rotavirus A	9,100 (13.60)	3,479 (28.09) **	1,267 (16.06)	312 (24.86) **	2,469 (24.91)	1,035 (37.45) **	3,857 (24.21)	1,866 (39.67) **	355 (8.65)	87 (12.74)	854 (3.99)	129 (5.76) **	298 (3.86)	50 (6.78)
Norovirus	6,857 (10.25)	1,905 (15.38) **	660 (8.36)	150 (11.95) **	1,142 (11.52)	505 (18.27) **	1,785 (11.20)	711 (15.11) **	365 (8.90)	97 (14.20) **	2,215 (10.36)	337 (15.04) **	690 (8.94)	105 (14.23) **
Adenovirus	2,097 (3.13)	487 (3.93) **	335 (4.25)	70 (5.58) *	487 (4.91)	124 (4.49)	851 (5.34)	222 (4.72)	128 (3.12)	21 (3.07)	206 (0.96)	29 (1.29)	90 (1.17)	21 (2.85)
Astrovirus	1,597 (2.39)	374 (3.02) **	251 (3.18)	63 (5.02)	270 (2.72)	99 (3.58) *	433 (2.72)	138 (2.93)	112 (2.73)	19 (2.78)	402 (1.88)	41 (1.83)	129 (1.67)	14 (1.90)
Sapovirus	989 (1.48)	213 (1.72) *	66 (0.84)	22 (1.75) **	152 (1.53)	51 (1.85)	339 (2.13)	92 (1.96)	49 (1.19)	12 (1.76)	310 (1.45)	29 (1.29)	73 (0.95)	7 (0.95)
Rotavirus B	187 (0.28)	46 (0.37)	23 (0.29)	5 (0.40)	34 (0.34)	10 (0.36)	74 (0.46)	27 (0.57)	13 (0.32)	1 (0.15)	30 (0.14)	2 (0.09)	13 (0.17)	1 (0.14)
Rotavirus C	152 (0.23)	47 (0.38) **	24 (0.30)	4 (0.32)	22 (0.22)	13 (0.47) *	34 (0.21)	20 (0.43) *	6 (0.15)	1 (0.15)	43 (0.20)	6 (0.27)	23 (0.30)	3 (0.41)
Bacterium	15,642 (17.05)	2,549 (17.76) *	719 (8.11)	119 (8.76)	1,328 (13.67)	338 (13.39)	2,865 (17.48)	737 (17.70)	1,053 (18.10)	187 (21.57) *	7,565 (20.08)	931 (22.55)	2,112 (15.90)	237 (18.11) *
NTS	4,148 (4.52)	1,000 (6.97) **	258 (2.91)	54 (3.97) *	625 (6.43)	199 (7.88) **	1,083 (6.61)	394 (9.46) **	247 (4.25)	57 (6.57) **	1,453 (3.86)	226 (5.47) **	482 (3.63)	70 (5.35) **
DEC	6,371 (6.94)	827 (5.76) **	313 (3.53)	55 (4.05)	549 (5.65)	115 (4.56) *	1,077 (6.57)	200 (4.80) **	398 (6.84)	47 (5.42)	3,144 (8.34)	323 (7.82)	890 (6.70)	87 (6.65)
<i>V.parahaemolyticus</i>	1,917 (2.09)	325 (2.26)	21 (0.24)	0 (0.00)	11 (0.11)	1 (0.04)	26 (0.16)	3 (0.07)	52 (0.89)	7 (0.81)	1,566 (4.16)	272 (6.59) **	241 (1.81)	42 (3.21) **
<i>Shigella</i>	1,397 (1.52)	263 (1.83) **	48 (0.54)	5 (0.37)	60 (0.62)	19 (0.75)	436 (2.66)	116 (2.79)	192 (3.30)	60 (6.92) **	495 (1.31)	52 (1.26)	166 (1.25)	11 (0.84)
<i>A. hydrophila</i>	823 (0.90)	86 (0.60)	48 (0.54)	4 (0.29)	65 (0.67)	6 (0.24) *	106 (0.65)	16 (0.38) *	36 (0.62)	5 (0.58)	415 (1.10)	41 (0.99)	153 (1.15)	14 (1.07)
<i>C.jejuni</i>	901 (0.98)	81 (0.56) **	23 (0.26)	1 (0.07)	45 (0.46)	7 (0.28)	176 (1.07)	22 (0.53) **	95 (1.63)	14 (1.61)	425 (1.13)	29 (0.70) *	137 (1.03)	8 (0.61)
<i>P. shigelloides</i>	406 (0.44)	49 (0.34)	3 (0.03)	2 (0.15)	10 (0.10)	2 (0.08)	13 (0.08)	1 (0.02)	17 (0.29)	2 (0.23)	290 (0.77)	36 (0.87)	73 (0.55)	6 (0.46)
<i>C. coli</i>	185 (0.20)	16 (0.11) *	5 (0.06)	0 (0.00)	14 (0.14)	5 (0.20)	41 (0.25)	4 (0.10)	25 (0.43)	2 (0.23)	77 (0.20)	3 (0.07)	23 (0.17)	2 (0.15)
<i>V. cholerae</i>	198 (0.22)	13 (0.09) **	2 (0.02)	0 (0.00)	4 (0.04)	0 (0.00)	13 (0.08)	1 (0.02)	7 (0.12)	0 (0.00)	141 (0.37)	10 (0.24)	31 (0.23)	2 (0.15)
<i>Y. enterocolitica</i>	220 (0.24)	12 (0.08)	14 (0.16)	0 (0.00)	20 (0.21)	0 (0.00) *	62 (0.38)	4 (0.10) **	23 (0.40)	2 (0.23)	71 (0.19)	4 (0.10)	30 (0.23)	2 (0.15)

Supplementary table 3 (Continued)

	Sex				Residence				Season of infection			
	Male		Female		Urban		Rural		Cold		Warm	
	Mild	MSD	Mild	MSD	Mild	MSD	Mild	MSD	Mild	MSD	Mild	MSD
Virus	11,523 (29.58)	3,493 (47.79) **	7,451 (26.63)	2,259 (44.51) **	14,728 (27.66)	3,755 (43.49) **	3,201 (31.47)	1,737 (54.47) **	10,426 (38.20)	3,608 (56.85) **	8,548 (21.57)	2,144 (35.51) **
Rotavirus A	5,627 (14.45)	2,158 (29.53) **	3,473 (12.41)	1,321 (26.03) **	7,201 (13.53)	2,181 (25.26) **	1,492 (14.67)	1,138 (35.69) **	6,043 (22.14)	2,568 (40.47) **	3,057 (7.71)	911 (15.09) **
Norovirus	4,140 (10.63)	1,139 (15.58) **	2,717 (9.71)	766 (15.09) **	5,346 (10.04)	1,365 (15.81) **	1,183 (11.63)	462 (14.49) **	3,152 (11.55)	927 (14.61) **	3,705 (9.35)	978 (16.20) **
Adenovirus	1,264 (3.24)	300 (4.10)	833 (2.98)	187 (3.68) **	1,449 (2.72)	285 (3.30) **	414 (4.07)	176 (5.52)	781 (2.86)	207 (3.26)	1,316 (3.32)	280 (4.64) **
Astrovirus	929 (2.38)	230 (3.15)	668 (2.39)	144 (2.84)	1,130 (2.12)	208 (2.41)	357 (3.51)	149 (4.67) **	843 (3.09)	208 (3.28)	754 (1.90)	166 (2.75) **
Sapovirus	617 (1.58)	116 (1.59)	372 (1.33)	97 (1.91) **	729 (1.37)	138 (1.60)	178 (1.75)	62 (1.94)	523 (1.92)	122 (1.92)	466 (1.18)	91 (1.51) *
Rotavirus B	117 (0.30)	34 (0.47) *	70 (0.25)	12 (0.24)	132 (0.25)	22 (0.25)	42 (0.41)	18 (0.56)	97 (0.36)	30 (0.47)	90 (0.23)	16 (0.26)
Rotavirus C	108 (0.28)	37 (0.51) **	44 (0.16)	10 (0.20)	118 (0.22)	19 (0.22)	32 (0.31)	25 (0.78)	51 (0.19)	19 (0.30)	101 (0.25)	28 (0.46) **
Bacterium	8,682 (16.65)	1,364 (17.02)	6,960 (17.57)	1,185 (18.70) *	12,017 (17.35)	1,746 (17.55)	3,025 (16.52)	721 (18.63) **	2,758 (8.83)	568 (9.41)	12,884 (21.30)	1,981 (23.82) **
NTS	2,276 (4.37)	589 (7.35) **	1,872 (4.73)	411 (6.48) **	3,143 (4.54)	667 (6.70) **	819 (4.47)	287 (7.42) **	740 (2.37)	219 (3.63) **	3,408 (5.63)	781 (9.39) **
DEC	3,519 (6.75)	441 (5.50) **	2,852 (7.20)	386 (6.09) **	4,952 (7.15)	576 (5.79) **	1,133 (6.19)	234 (6.05)	1,038 (3.32)	216 (3.58)	5,333 (8.82)	611 (7.35) **
<i>V.parahaemolyticus</i>	986 (1.89)	161 (2.01)	931 (2.35)	164 (2.59)	1,694 (2.45)	282 (2.83) *	191 (1.04)	36 (0.93)	97 (0.31)	17 (0.28)	1,820 (3.01)	308 (3.70)
<i>Shigella</i>	840 (1.61)	131 (1.63)	557 (1.41)	132 (2.08) **	620 (0.90)	104 (1.05)	714 (3.90)	155 (4.01)	207 (0.66)	63 (1.04) **	1,190 (1.97)	200 (2.41) **
<i>A. hydrophila</i>	461 (0.88)	36 (0.45) **	362 (0.91)	50 (0.79)	611 (0.88)	64 (0.64) *	199 (1.09)	19 (0.49)	138 (0.44)	19 (0.31)	685 (1.13)	67 (0.81) **
<i>C.jejuni</i>	540 (1.04)	39 (0.49) **	361 (0.91)	42 (0.66) *	854 (1.23)	75 (0.75) **	40 (0.22)	3 (0.08)	394 (1.26)	31 (0.51) **	507 (0.84)	50 (0.60) *
<i>P. shigelloides</i>	221 (0.42)	20 (0.25) *	185 (0.47)	29 (0.46)	366 (0.53)	42 (0.42)	37 (0.20)	7 (0.18)	38 (0.12)	5 (0.08)	368 (0.61)	44 (0.53)
<i>C. coli</i>	107 (0.21)	6 (0.07) *	78 (0.20)	10 (0.16)	180 (0.26)	9 (0.09) **	5 (0.03)	4 (0.10)	79 (0.25)	4 (0.07) **	106 (0.18)	12 (0.14)
<i>V. cholerae</i>	105 (0.20)	6 (0.07) *	93 (0.23)	7 (0.11) *	168 (0.24)	7 (0.07)	24 (0.13)	5 (0.13)	12 (0.04)	1 (0.02)	186 (0.31)	12 (0.14) **
<i>Y. enterocolitica</i>	122 (0.23)	8 (0.10) *	98 (0.25)	4 (0.06) **	161 (0.23)	10 (0.10) **	29 (0.16)	2 (0.05)	102 (0.33)	4 (0.07)	118 (0.20)	8 (0.10) *

Data are presented as n (%). Chi-square test or Fisher's exact test were used for comparisons among different groups. *, p<0.05; **, p<0.01. Virus: positive rate of any virus; Bacterium: positive rate of any bacteria. Positive rate was calculated by taking the positive number of each pathogen as the numerator and the total number of cases that underwent the tests for each specific pathogen as denominator. The viral positive rate of 12,384 MSD patients who had all the seven viral pathogens tested; the bacterial positive rate of 14,352 MSD patients who had all the ten bacterial pathogens tested. DEC=diarrheagenic *Escherichia coli*; NTS=nontyphoidal *Salmonella*

Supplementary table 4. Co-infection rate compared between mild diarrhea and MSD patients by age.

	Co-infection			Viral-bacterial			Bacterial-bacterial			Viral-viral		
	Mild	MSD	p value	Mild	MSD	p value	Mild	MSD	p value	Mild	MSD	p value
Total	2,066 (5.25)	570 (8.78)	<0.0001	905 (2.30)	211 (3.25)	<0.0001	323 (0.82)	43 (0.66)	0.2108	838 (2.13)	316 (4.87)	<0.0001
Age group, n (%)												
<6 months	189 (5.57)	41 (6.79)	0.2753	53 (1.56)	9 (1.49)	>0.9999	6 (0.18)	0 (0.00)	0.6000	130 (3.83)	32 (5.30)	0.1156
6–11 months	295 (7.32)	135 (11.19)	<0.0001	111 (2.76)	47 (3.90)	0.0526	11 (0.27)	3 (0.25)	>0.9999	173 (4.29)	85 (7.05)	<0.0001
1–4 years	551 (7.93)	211 (10.51)	<0.0001	214 (3.08)	62 (3.09)	>0.9999	28 (0.4)	3 (0.15)	0.1366	309 (4.45)	146 (7.27)	<0.0001
5–17 years	94 (4.19)	23 (6.93)	0.0365	48 (2.14)	9 (2.71)	0.6464	10 (0.45)	2 (0.60)	0.6608	36 (1.61)	12 (3.61)	0.0210
18–59 years	755 (4.52)	127 (7.15)	<0.0001	387 (2.32)	65 (3.66)	<0.0001	222 (1.33)	32 (1.80)	0.1285	146 (0.87)	30 (1.69)	0.0012
≥60 years	182 (3.01)	33 (5.83)	<0.0001	92 (1.52)	19 (3.36)	0.0021	46 (0.76)	3 (0.53)	0.7965	44 (0.73)	11 (1.94)	0.0061
Season of infection, n (%)												
Cold	821 (5.54)	311 (10.01)	<0.0001	299 (2.02)	86 (2.77)	0.0107	25 (0.17)	2 (0.06)	0.2109	497 (3.35)	223 (7.18)	<0.0001
Warm	1245 (5.07)	259 (7.65)	<0.0001	606 (2.47)	125 (3.69)	<0.0001	298 (1.21)	41 (1.21)	>0.9999	341 (1.39)	93 (2.75)	<0.0001

Data are presented as n (%), Chi square test or Fisher's exact test were used for comparisons for MSD and mild diarrhea groups

Supplementary table 5. Coinfection patterns for different age groups between MSD and mild diarrhea patients. Only the top 5 pairs of the coinfection pathogens were listed.

	Co-infection rate (%)		Co-infection rate (%)		Co-infection rate (%)
<6 month					
Total (n=294)		MSD (n=45)		Mild diarrhea (n=249)	
Rotavirus A-norovirus	55 (18.71)	Rotavirus A-norovirus	9 (20.00)	Rotavirus A-norovirus	46 (18.47)
Rotavirus A-astrovirus	34 (11.56)	Rotavirus A-adenovirus	7 (15.56)	Rotavirus A-astrovirus	30 (12.05)
Norovirus-astrovirus	31 (10.54)	Norovirus-DEC	5 (11.11)	Norovirus-astrovirus	28 (11.24)
Norovirus-adenovirus	26 (8.84)	Rotavirus A-sapovirus	4 (8.89)	Norovirus-adenovirus	19 (7.63)
Rotavirus A-adenovirus	20 (6.80)	Rotavirus A-astrovirus	4 (8.89)	Rotavirus A-adenovirus	18 (7.23)
6–11 month					
Total (n=580)		MSD (n=173)		Mild diarrhea (n=407)	
Rotavirus A-norovirus	119 (20.52)	Rotavirus A-norovirus	46 (26.59)	Rotavirus A-norovirus	73 (17.94)
Rotavirus A-adenovirus	48 (8.28)	Norovirus-adenovirus	18 (10.40)	Rotavirus A-adenovirus	33 (8.11)
Norovirus-adenovirus	45 (7.76)	Rotavirus A-adenovirus	15 (8.67)	Norovirus-DEC	29 (7.13)
Norovirus-DEC	38 (6.55)	Rotavirus A-DEC	12 (6.94)	Norovirus-adenovirus	27 (6.63)
Norovirus-NTS	37 (6.38)	Norovirus-astrovirus	11 (6.36)	Norovirus-NTS	26 (6.39)
1–4 years					
Total (n=1,001)		MSD (n=274)		Mild diarrhea (n=727)	
Rotavirus A-norovirus	182 (18.18)	Rotavirus A-norovirus	67 (24.45)	Rotavirus A-norovirus	115 (15.82)
Rotavirus A-adenovirus	86 (8.59)	Rotavirus A-adenovirus	31 (11.31)	Norovirus-DEC	61 (8.39)
Norovirus-adenovirus	77 (7.69)	Norovirus-adenovirus	27 (9.85)	Rotavirus A-adenovirus	55 (7.57)
Norovirus-DEC	74 (7.39)	Rotavirus A-astrovirus	20 (7.30)	Norovirus-adenovirus	50 (6.88)
Rotavirus A-astrovirus	54 (5.39)	Rotavirus A-DEC	20 (7.30)	Rotavirus A-astrovirus	34 (4.68)
5–17 years					
Total (n=142)		MSD (n=27)		Mild diarrhea (n=115)	
Rotavirus A-norovirus	12 (8.45)	Rotavirus A-norovirus	4 (14.81)	Norovirus-DEC	9 (7.83)
Norovirus-DEC	11 (7.75)	Norovirus-astrovirus	3 (11.11)	Rotavirus A-norovirus	8 (6.96)
Norovirus-astrovirus	10 (7.04)	Norovirus-adenovirus	2 (7.41)	Rotavirus A-DEC	7 (6.09)
Rotavirus A-DEC	8 (5.63)	Norovirus-sapovirus	2 (7.41)	Norovirus-astrovirus	7 (6.09)
Norovirus-adenovirus	8 (5.63)	Norovirus- DEC	2 (7.41)	Rotavirus A-astrovirus	6 (5.22)
18–60 years					
Total (n=1,019)		MSD (n=142)		Mild diarrhea (n=877)	
Norovirus-DEC	177 (17.37)	Norovirus- DEC	29 (20.42)	Norovirus-DEC	148 (16.88)
Rotavirus A-norovirus	55 (5.40)	Rotavirus A-norovirus	11 (7.75)	Rotavirus A-norovirus	44 (5.02)
Rotavirus A-DEC	50 (4.91)	Rotavirus A-DEC	8 (5.63)	Rotavirus A-DEC	42 (4.79)
DEC- <i>V. parahaemolyticus</i>	43 (4.22)	DEC- <i>V. parahaemolyticus</i>	8 (5.63)	Norovirus-NTS	36 (4.10)
Norovirus-NTS	39 (3.83)	DEC-C. jejuni	7 (4.93)	DEC- <i>V. parahaemolyticus</i>	35 (3.99)
≥60 years					
Total (n=258)		MSD (n=46)		Mild diarrhea (n=212)	
Norovirus-DEC	34 (13.18)	Norovirus-DEC	7 (15.22)	Norovirus-DEC	27 (12.74)
Norovirus-astrovirus	20 (7.75)	Norovirus-adenovirus	6 (13.04)	Norovirus-astrovirus	16 (7.55)
Rotavirus A-DEC	17 (6.59)	Rotavirus A-DEC	5 (10.87)	Rotavirus A-DEC	12 (5.66)
Rotavirus A-norovirus	14 (5.43)	Norovirus-astrovirus	4 (8.70)	DEC- <i>A. hydrophila</i>	12 (5.66)
DEC- <i>A. hydrophila</i>	13 (5.04)	Rotavirus A-norovirus	3 (6.52)	Rotavirus A-norovirus	11 (5.19)

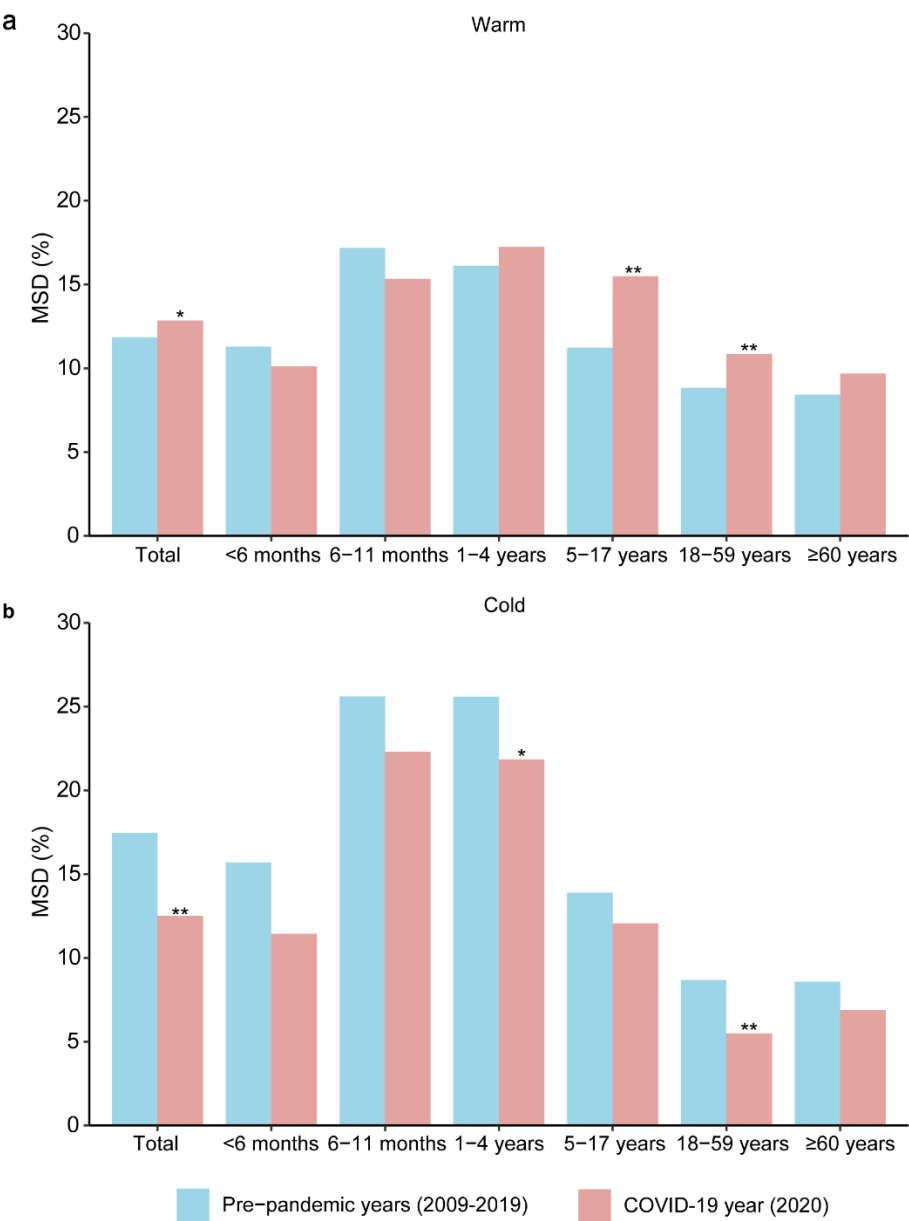
Supplementary table 6. The association between MSD and age, sex, season of infection, pathogen prevalence.

	MSD (%)	Univariate analysis		Multivariate analysis	
		Crude OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Children and adolescents <18 years (n=4,015)					
Sex					
Female	1,533 (20.11)	Reference		Reference	
Male	2,482 (20.17)	1.00 (0.94–1.08)	0.9096	1.00 (0.93–1.07)	0.9743
Residence					
Urban	2,734 (18.42)	Reference		Reference	
Rural	1,281 (25.19)	1.49 (1.38–1.61)	<0.0001	1.49 (1.38–1.61)	<0.0001
Season of infection					
Warm	1,734 (15.94)	Reference		Reference	
Cold	2,281 (25.20)	1.78 (1.66–1.91)	<0.0001	1.52 (1.41–1.64)	<0.0001
Pathogen prevalence					
All negative	1,714 (14.77)	Reference		Reference	
Rotavirus A-DEC	32 (36.78)	3.36 (2.16–5.20)	<0.0001	2.96 (1.90–4.61)	<0.0001
Rotavirus A	1,010 (35.33)	3.15 (2.87–3.46)	<0.0001	2.77 (2.52–3.05)	<0.0001
Rotavirus A-norovirus	126 (34.24)	3.00 (2.41–3.75)	<0.0001	2.60 (2.08–3.26)	<0.0001
Norovirus-adenovirus	38 (32.48)	2.77 (1.88–4.10)	<0.0001	2.51 (1.69–3.71)	<0.0001
Norovirus	510 (28.11)	2.26 (2.01–2.53)	<0.0001	2.21 (1.97–2.48)	<0.0001
Rotavirus A-astrovirus	25 (28.41)	2.29 (1.44–3.65)	0.0005	1.99 (1.24–3.18)	0.0041
Norovirus-astrovirus	19 (27.14)	2.15 (1.27–3.65)	0.0046	1.93 (1.13–3.29)	0.0155
Rotavirus A-adenovirus	33 (27.27)	2.16 (1.45–3.24)	0.0002	1.92 (1.28–2.88)	0.0017
NTS	160 (24.73)	1.90 (1.57–2.28)	<0.0001	2.09 (1.73–2.52)	<0.0001
Norovirus-DEC	25 (21.37)	1.57 (1.00–2.45)	0.0477	1.64 (1.05–2.57)	0.0298
Adenovirus	99 (16.42)	1.13 (0.91–1.41)	0.2689	1.17 (0.94–1.46)	0.1719
<i>Shigella</i>	22 (20.95)	1.53 (0.95–2.45)	0.0784	1.49 (0.92–2.40)	0.1015
Astrovirus	71 (17.79)	1.25 (0.96–1.62)	0.0962	1.16 (0.89–1.51)	0.2586
Sapovirus	45 (15.85)	1.09 (0.79–1.50)	0.6158	1.04 (0.75–1.43)	0.8276
DEC	86 (13.29)	0.88 (0.70–1.12)	0.3003	0.98 (0.77–1.23)	0.8365
Adults ≥18 years (n=2,203)					
Sex					
Female	1,218 (10.40)	Reference		Reference	
Male	985 (8.09)	0.76 (0.69–0.83)	<0.0001	0.76 (0.70–0.83)	<0.0001
Residence					
Urban	1,925 (9.24)	Reference		Reference	
Rural	278 (9.07)	0.98 (0.86–1.12)	0.7571	1.05 (0.92–1.20)	0.4573
Season of infection					
Warm	1,473 (9.41)	Reference		Reference	
Cold	730 (8.86)	0.94 (0.85–1.03)	0.1570	0.93 (0.84–1.02)	0.1245
Pathogen prevalence					
All negative	1,329 (7.86)	Reference		Reference	
Rotavirus A-DEC	12 (18.75)	2.71 (1.44–5.08)	0.0020	2.68 (1.42–5.04)	0.0022
<i>V. parahaemolyticus</i>	112 (17.61)	2.51 (2.03–3.10)	<0.0001	2.44 (1.97–3.03)	<0.0001
Norovirus-DEC	36 (17.06)	2.41 (1.68–3.47)	<0.0001	2.42 (1.69–3.49)	<0.0001
Adenovirus	21 (15.56)	2.16 (1.35–3.45)	0.0013	2.11 (1.32–3.38)	0.0018
NTS	110 (15.28)	2.11 (1.71–2.61)	<0.0001	2.09 (1.69–2.58)	<0.0001
Norovirus	276 (13.87)	1.89 (1.64–2.17)	<0.0001	1.93 (1.68–2.22)	<0.0001
Rotavirus A	95 (13.31)	1.80 (1.44–2.25)	<0.0001	1.83 (1.46–2.30)	<0.0001
DEC	144 (9.39)	1.21 (1.01–1.46)	0.0345	1.19 (0.99–1.42)	0.0658
Astrovirus	26 (8.87)	1.14 (0.76–1.71)	0.5220	1.13 (0.75–1.70)	0.5459
<i>A. hydrophila</i>	22 (8.40)	1.08 (0.69–1.67)	0.7473	1.06 (0.68–1.64)	0.8082

Sapovirus	13 (5.00)	0.62 (0.35–1.08)	0.0916	0.63 (0.36–1.11)	0.1097
<i>C. jejuni</i>	7 (4.46)	0.55 (0.26–1.17)	0.1200	0.57 (0.26–1.21)	0.1422

Bold font indicates P value <0.05. Results are not shown when the number of positive pathogens is less than 70 in children and adolescents <18 years or adults ≥18 years. DEC=diarrheagenic *Escherichia coli*; NTS=nontyphoidal *Salmonella*

Supplementary figure 1. Comparison of the proportion of MSD in different age groups in each season between pre-pandemic years (2009–2019) and the COVID-19 pandemic year (2020). Blue and pink bar indicates the proportion of MSD of different age groups in each season during the pre-pandemic years (2009–2019) and during the first COVID-19 pandemic year (2020), respectively. Statistically significant changes were marked with asterisks (* $p<0.05$; ** $p<0.01$ based on chi-square test or Fisher’s exact test). (A) Comparison of the proportion of MSD in different age groups in warm season between pre-pandemic years (2009–2019) and COVID-19 pandemic year (2020). (B) Comparison of the proportion of MSD in different age groups in cold season between pre-pandemic years (2009–2019) and COVID-19 pandemic year (2020).



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